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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,936	11/07/2001	Olle Korsgren	KORSGREN-1	9165

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EXAMINER	
JAGOE, DONNA A	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 03/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/890,936	KORSGREN ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,8,9 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,8,9 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The amendment filed 30 June 2005 has been received and entered. Claims 4, 8, 9 and 11 have been amended and claims 1-3, 5-7, 10 and 12-13 have been canceled. New claims 14-25 have been added.

Election/Restrictions

Newly submitted claims 14-25 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: applicant has received an action on the merits for the invention of a method comprising transplantation of insulin producing cells in the form of isolated islets wherein the islets are modified by adsorption with a clotting inhibiting agent. New claims 14-24 are drawn to the isolated islets, which are separate and distinct from the method of using the isolated islets. New claim 25 is drawn to a method of production of a composition for treatment of insulin dependent diabetes mellitus comprising coating isolated islets with a clotting inhibiting agent, which is separate and distinct from the method of transplanting isolated modified islet cells.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 14-25 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 4, 8, 9 and 11 are pending in this application.

Rejection of claims 1, 4 and 10 under 35 USC §112 1st paragraph for the proviso that "the isolated islets are not artificially encapsulated" is no longer maintained in view of the amendment/cancellation of the claims.

Rejection of claims 1, 2, 4-8 and 10-12 under 35 USC §112 1st paragraph for recitation of the word "preventing" is no longer maintained in view of the amendment/cancellation of the claims.

Rejection of claims 1, 4, 12 and 13 under 35 USC §112 2nd paragraph for recitation of "said isolated islets" is no longer maintained in view of the amendment/cancellation of the claims.

Rejection of claims 2, 5, 6, 7 and 9 under 35 USC §112 2nd paragraph is no longer maintained in view of the cancellation of the claims.

Art Rejections of Record

Claims 1-4 and 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Wagner et al. DE 196 23 440 A 1.

Wagner et al. teach method of use of anticoagulants such as heparin, hirudin and Marcumar and derivatives thereof in connection with transplantation of insulin producing cells such as islets of Langerhans (see claim 8). The cells may be in the form of microencapsulated islets (see figure 1 and claim 10) and where immunosuppression can be an issue, see "Islet Transplant Info" that teaches that immunosuppression and/or appropriate drugs, such as Zenapax should be used to address the issue. The abstract for Wagner et al. teach that the immobilized material is insulin, proinsulin and/or organ

cells of xenogenic or autogenic origin (islets of Langerhans, etc.) and the system contains an agent to inhibit or suppress blood agglutination, agglomeration antagonists, heparin, hirudin, marcumar and their derivatives. Wagner discloses that the islets *may* be microencapsulated. Additionally, if the cells are microencapsulated, they are first mixed with the anticoagulant material, thus anticipated the claims of the instant application.

The rejection of claims 1 and 5-7, rejected under 35 U.S.C. 102(b) as being anticipated by Lenschow et al. (Science 7 Aug 1992 Vol. 257 ages 789-792) is no longer maintained in view of the cancellation of the claims.

Claims 1-4, 10 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Soon-Shiong et al. U.S. 5,705,270 A.

Soon-Shiong et al. teach microcapsules containing biological material such as islet of Langerhans cells coated with polymerizable materials (see abstract, see also claim 3). The microcapsules are covalently linked with heparin (see claim 5). Soon-Shiong et al. teach encapsulation of islets of Langerhans for treatment of diabetes (column 4, lines 1-4) to prevent the detrimental effects of capsule instability on the encapsulated biologically active material e.g. loss of immunoprotection for the encapsulated material is minimized (column 3, lines 61-66). Additionally, note that there is no provision in the instant claims that deals with the immunosuppression issue, without which, the transplanted islet cells would be rejected (see Islet Transplant Info).

The instant specification describes immobilizing heparin according to a method developed by Corline Systems AB disclosed in WO 93/05793 (page 4 of the instant specification). The heparin in WO 93/05793 appears to be immobilized (conjugated) with a polymer comprising a substantially straight-chained organic homo or hetero polymer having a number of functional groups distributed along the polymer backbone chain via which groups at least about 20 molecules (see page 7 of WO 93/05793). While applicant asserts that the heparin is not in microcapsules, it appears that it is similarly coated and as such, must form micro (or macro) capsules if applicant has followed the technique of Corline Systems AB as recited in applicants specification.

Response to Arguments

Applicant's arguments filed June 30, 2005 have been fully considered but they are not persuasive. The rejections above are maintained and hereby repeated.

Regarding Wagner, applicant asserts that microcapsules are used. In response, applicants' attention is drawn to the claims of Wagner wherein the Islets of Langerhans (claim 3) can be used as organic immobilized materials. The immobilization of the islets is with the help of synthetic **or** natural high molecular weight compounds (claim 4). The natural high molecular weight compounds are inter alia heparin (see claim 6). Again, while applicant asserts that the heparin recited instantly is not in microcapsules, it appears that it is similarly coated, and as such, must form micro (or macro) capsules if applicant has followed the technique of Corline Systems AB as recited in applicants specification on pages 4-5.

Regarding the response to the Declaration submitted March 2, 2004, applicants bristle about the fact that the PTO has "ignored" statements of fact. The declaration states that the coating is not the same as Wagner and Soon-Shiong because it does not result in encapsulation. Applicant has yet to respond to the fact that the instant specification points to encapsulation on page 4 to 5 wherein the polymer surface of the tubing is modified with a high molecular weight amine compound to add primary amine groups to the surface. A soluble conjugate is prepared by covalent binding of approximately 60 ml of heparin per mole of a straight chained polyallylamine is irreversibly bonded onto the amine surface of the tubings. The modified heparin would encapsulate the islets as in Wagner. Further, Wagner is not encapsulated in every aspect of the invention. It reads that it "**may**" be encapsulated. Either way, the islet cells are added to a high molecular weight substance, such as heparin. It is unclear how the heparin-alginate conjugate of the Corline system differs from the heparin/alginate system of Soon-Shiong (see abstract). Applicant asserts that evidence submitted by way of the Declaration was ignored. See response in office action dated March 31, 2005. Evidence was not ignored, as stated in the office action dated March 31, 2005, it was **insufficient** to overcome the rejection of the claims over the prior art of record.

Regarding the Soon-Shiong rejection, applicant asserts that the objective is to provide an encapsulation which allows delivery of substances from the insides of the capsule. Soon-Shiong et al. teach microcapsules containing biological material such as islet of Langerhans cells coated with polymerizable materials (see abstract, see also

claim 3). The microcapsules are covalently linked with heparin (see claim 5). Soon-Shiong et al. teach encapsulation of islets of Langerhans for treatment of diabetes (column 4, lines 1-4) to prevent the detrimental effects of capsule instability on the encapsulated biologically active material e.g. loss of immunoprotection for the encapsulated material is minimized (column 3, lines 61-66). It is unclear how the Corline system of alginate-heparin differs from the Soon-Shiong et al. system of encapsulation of islets of Langerhans.

Rejection of claim 5 under 35 USC §103 is no longer maintained in view of the cancellation of claim 5.

New Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 4, 8, 9 and 11 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Bennet et al. (Incompatibility Between Human Blood and Isolated Islets of Langerhans: A Finding With Implications for Clinical Intraportal Islet Transplantation, Diabetes, 1999 Vol. 48 pages 1907-1914).

Bennet et al. teach transplantation of isolated islets of Langerhans with heparin and optionally the complement inhibitor sCR-1 (page 1908, col. 2, 3rd full paragraph). Bennet et al. teach the disruption of the integrity of the islets could be prevented by the

addition of heparin in combination with the complement inhibitor, soluble complement receptor 1 (sCR-1) (page 1908, column 1, 2nd full paragraph to the 3rd full paragraph). Bennet et al. state that "most centers performing allogenic islet transplantation today use systemic heparin at the time of transplantation. Heparin is usually administered as a bolus dose. Addition of heparin prevented coagulation, reduced cell consumption and to a large degree, inhibited complement activation, but the addition of heparin in combination with sCR-1 effectively inhibited coagulation and complement activation (page 1913, 1st full paragraph).

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Christopher S. F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Donna Jagoe
Patent Examiner
Art Unit 1614

March 13, 2006

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